

What is Claimed:

1. A method of identifying an individual at an  
5 increased risk of breast carcinoma associated with a  
polymorphism in a gene, comprising determining the MHC  
genotype of an individual and identifying polymorphisms  
associated with the predisposition or susceptibility to  
breast carcinoma.
- 10 2. The method of claim 1 wherein the polymorphism is  
on the TNF- $\alpha$  gene at the -308 locus.
3. The method of claim 1 wherein the polymorphism is  
15 on the HSP70-2 gene at the 1267 locus.
4. A method of identifying a predisposition or  
susceptibility to breast carcinoma, the method comprising  
determining whether the individual possesses a polymorphic  
20 risk version of the TNF- $\alpha$  gene, wherein the risk version  
has an A at site at the -308 site, the method comprising:
- (a) digestion of corresponding PCR products with the  
endonuclease Nco I;
- (b) analysis of amplified fragments by agarose-gel  
25 electrophoresis, wherein the presence of Nco I site is  
indicated by the cleavage of the 107 bp amplified fragment  
to yield fragments of 87 bp and 20 bp, and wherein the two  
allelic forms of TNF- $\alpha$  corresponding to the presence or  
absence of NcoI are referred to as TNF-1 and TNF-2  
30 respectively;
- (c) identifying the presence of susceptibility to  
breast carcinomas greatest if that individual is homozygous  
for the polymorphic risk version of the gene at the -308  
site (TNF2/TNF2).
- 35 5. A method of identifying a predisposition or  
susceptibility to breast carcinoma, the method comprising

1040707, 040707

determining whether the individual possesses a polymorphic risk version of the HSP70-2 gene, wherein the risk version of the HSP70-2 gene lacks a *Pst* I site at the 1267 position, the method comprising:

5 (a) digestion of corresponding PCR products with *Pst* I;

(b) analysis of amplified fragments by agarose-gel electrophoresis, wherein the presence of the *Pst* I site is indicated by the cleavage of the 2075 bp amplified product  
10 to yield fragments of 1139 bp and 936 bp, and wherein the two allelic forms of HSP70-2 gene corresponding to the presence or absence of *Pst* I site are referred to as HSPP1 and HSPP2 respectively;

(c) identifying the presence of susceptibility to  
15 breast carcinomas greatest if that individual is homozygous for the polymorphic risk version of the gene at the 1267 site (P2/P2).

6. A method of managing and treating patients with a  
20 predisposition to breast carcinoma, comprising determining whether the individual possesses a polymorphism in an MHC gene associated with breast carcinoma, wherein the management and treatment of such patient having such polymorphism are promptly treated and managed as patients  
25 having a predisposition to breast carcinoma.

7. The method of claim 6 wherein the polymorphism is located on the TNF- $\alpha$  gene at the -308 locus.

30 8. The method of claim 6 wherein the polymorphism is located on the HSP70-2 gene at the 1267 locus.

9. A method of screening to identify compounds which stimulate or inhibit the synthesis or action of a  
35 polymorphism in an MHC gene associated with breast carcinoma, comprising screening compounds with desired polymorphism sites and identifying those compounds which

act as agonists toward the sites and those compounds which inhibit activity as antagonists.

10. The method of claim 9 wherein the polymorphism  
5 site is selected from the group consisting of TNF- $\alpha$  and HSP70-2.

11. A agonist or antagonist identified by the method  
of claim 10.

10

12. A method of treating patients comprising  
identifying a patient with a predisposition to breast  
carcinoma by identifying polymorphisms in an MHC gene  
associated with breast carcinoma and administering to such  
15 patient an effective amount of an antagonist identified in  
claim 11 in a pharmaceutically acceptable carrier.

13. A method of predicting the clinical outcome of a  
breast carcinoma patient comprising determining whether the  
20 individual possesses a TNF2 homozygous genotype of the TNF- $\alpha$  gene at the -308 locus wherein the TNF-breast carcinoma-specific overall survival and disease-free survival are considered to be shortest in patients carrying the TNF2 homozygous genotype.

25

14. A method of predicting the clinical outcome of a  
breast carcinoma patient comprising determining whether the  
individual possesses a HSP70-2 homozygous genotype, wherein  
the survival rate is the longest in the group of breast-  
30 carcinoma patients carrying the HSP-P2 homozygous genotype.